REMARKS

Claims 1, 3, 4, 6-9, 11-13, 17, 19, 20, 22-25, and 38 were previously pending, of which claims 7-9 have been withdrawn from consideration. No claims are currently amended. No claims are currently canceled. No new claims are added. No new matter has been introduced. Upon entry of this Amendment, claims 1, 3, 4, 6-9, 11-13, 17, 19, 20, 22-25, and 38 remain pending, of which claims 7-9 have been withdrawn from consideration as being directed to non-elected species.

Withdrawn Rejections

Applicant acknowledges that the Examiner has withdrawn the previous rejection of claims 1, 3, 6, 10-12, 17, 19, 22-24, and 38 under 35 U.S.C. 102(b) as being anticipated by Larsen et al. (U.S. Patent No. 5,840,679) and in further evidence of Chen et al. (*Blood* 104:3233-3242, 2004).

Applicant acknowledges that the Examiner has withdrawn the previous rejection of claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25, and 38 under 35 U.S.C. 102(e) as being anticipated by Lazarovits et al. (US 2004/0002450) and as further evidenced by the Lin 132 Declaration.

Applicant acknowledges that the Examiner has withdrawn the previous rejection of claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25, and 38 under 35 U.S.C. 103(a) over Larsen et al. (*supra*) in view of Trembleau et al. (*J. Immunol.* 163:2960-2968, 1999), Yago et al. (*J. Immunol.* 161:1140-1145, 1998), Hirata et al. (*J. Exp. Med.* 192:1669-1675, 2000), and Cobbold et al. (U.S. Patent No. 6,056,956) and as further evidenced by Chen et al. (*supra*).

Applicant acknowledges that the Examiner has withdrawn the previous rejection of claims 1, 3, 4, 6, 10-13, 17, 19, 20, 22-25, and 38 under 35 U.S.C. 103(a) over Larsen et al. (*supra*) in view of Trembleau et al. (*supra*), Yago et al. (*supra*), Hirata et al. (*supra*), and Cobbold et al. (supra) and as further evidenced by Chen et al. (*supra*) and further in view of Snapp et al. (*Blood* 91:3233-3242, 2004) and/or Lazarovits et al. (*supra*) and as further evidenced by the Lin 132 Declaration.

Plenary Remarks

The Examiner's rejections and arguments continue to be difficult to understand, and in some instances irrelevant, because in several instances, as pointed out in detail below, they appear to concern previous versions of the claims (as well as earlier arguments in support of same) and/or subject matter not expressly claimed.

Priority

In Item 3 beginning on page 2 of the Office Action, the Examiner again asserted that the priority application USSN 60/310,196, filed 08/03/2001, does not appear to provide sufficient written description for the claimed invention. Applicant has addressed this issue previously and here again merely acknowledges that the Examiner has maintained this assertion and reiterated his reasoning that is based on earlier versions of the claims.

Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

In Item 4 beginning on page 5 of the Office Action, the Examiner again rejected claims 4 and 20 under 35 U.S.C. 112, first paragraph, for alleged lack of written description. These claims recite the limitation "an antibody that binds to the monoclonal antibody and induces cross-linking of a plurality of PSGL-1 antigens on the surface of the [T cell]." The Examiner correctly acknowledged on page 5 of the Office Action that the Applicant, in support of these claims, has previously pointed out two examples of cross-linking antibodies as claimed, i.e., anti-hamster Ig disclosed in Example 3 and anti-mouse Ig disclosed in Example 10 in the specification. The Examiner also correctly acknowledged on page 6 of the Office Action that Applicant has previously asserted that it would be appreciated that the claimed genus of cross-linking antibodies includes any suitable anti-isotype antibody, examples of which are so numerous in the prior art [as to not require specific disclosure]. Amendment of January 30, 2007, paragraph bridging pages 9-10.

On page 7 of the Office Action the Examiner asserted that the specification "does not provide sufficient ... blaze marks nor direction" for the instant methods encompassing the

above-mentioned limitation. Applicant respectfully disagrees. The Examiner apparently relies on In re Ruschig, 379 F.2d 990 (CCPA 1967) for the notion of sufficient blaze marks and direction to satisfy the written description requirement.[1] Such reliance is misplaced. That case concerned a patent application filed by Upjohn claiming a genus of certain chemical compounds known as benzene sulfonyl ureas for use in the treatment of diabetes. During prosecution of the application, Pfizer introduced to the market a particular species of benzene sulfonyl urea, chlorpropamide, and Upjohn sought to amend its claims in order to protect the use of chlorpropamide for the treatment of diabetes. Upjohn's disclosure included a generic structural formula with various R groups but no specific disclosure of the particular combination of R groups corresponding to chlorpropamide. The court held that while the structure of chlorpropamide was "derivable" from the disclosures of the various R groups, there was insufficient written description to support the single particular embodiment of chlorpropamide out of the more than half a million possible compounds encompassed by the disclosed generic structural formula and possible R groups.

In contrast, the instant claims concern, in pertinent part, a class of certain widely recognizable antibodies (not merely *agents*) capable of cross-linking other antibodies. Unlike In re Ruschig, the claims are not directed to a single particular species that is not specifically and unambiguously disclosed in the specification. Also unlike In re Ruschig, two specific examples of such antibodies are expressly disclosed in the specification. As Applicant previously pointed out, it is not necessary in this instance to have disclosed additional examples of such antibodies since a person of ordinary skill in the art clearly would have recognized Applicant was in possession of the claimed invention and could readily generate a list of additional cross-linking antibodies that would be expected to work as claimed.

Applicant respectfully asserts that the paragraph at the bottom of page 5 of the Office Action, which appears to suggest that Applicant relies on the original claim directed to cross-

[1] In the opinion by Judge Rich, "It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail or in finding one's way through the woods where the trails have disappeared – or have not yet been made, which is more the case here – to be confronted simply by a large number of unmarked trees. Appellants are pointing to trees. We are looking for blaze marks which single out particular trees. We see none. *Ibid.* at 994-995.

linking *agent* to support the current claim directed to cross-linking *antibody*, overlooks the merits of what is actually disclosed. As noted above, written support for antibody is provided by express examples. Example 3 at page 20 of the specification discloses, "Activated T cells were harvested, resuspended, and challenged with TAB4 monoclonal antibody or control hamster IgG in the presence of anti-hamster IgG antibody as cross-linker." [Emphasis added.] Similarly, Example 10 at page 26 of the specification discloses, "Activated T cells were harvested and then challenged with anti-PSGL-1 in the presence of IL-2 and cross-linking antibodies." [Emphasis added.] Example 10 then goes on to make multiple references to "cross-linker rabbit anti-mouse Ig" and "crosslinker". There can be no question that the exemplified antibodies are species of the claimed cross-linking antibodies.

Similarly, the third paragraph on page 6 of the Office Action makes reference to Applicant's "reliance on a generic disclosure (e.g. agent)" as insufficient basis for the claimed "generic 'antibody that binds to the monoclonal antibody and induces the cross-linking of a plurality of PSGL-1 antigen on the surface of the T cell', as currently claimed." [Emphasis in original.] This assertion by the Examiner mischaracterizes and seemingly discredits Applicant's actual arguments in support of what is currently claimed. Applicant is relying on actual, specific examples and species of cross-linking antibody in support of the claimed genus of antibody, not on a generic disclosure of *agent*.

Furthermore, the fourth paragraph on page 6 of the Office Action appears to suggest that Applicant believes that a generic or sub-generic disclosure can support a species in absence of specific description of that species. Applicant, in response, respectfully submits that while it is true that "antibody" may be considered to be a subgenus relative to "agent", Applicant is not suggesting that "agent" supports "antibody" in absence of a specific description and/or exemplification of antibody. Rather, Applicant is urging the Examiner to accept that the disclosure of two species of cross-linking antibody provides sufficient written description to support the currently claimed genus of cross-linking antibodies.

The Examiner cites In re Smith, 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05 in the fourth paragraph on page 6 of the Office Action for the proposition that "[I]t cannot be

said that [a] subgenus is necessarily described by a genus encompassing it and a species upon which it reads." [Emphasis added.] Applicant agrees with the proposition, but not with the Examiner's application of the proposition to this particular set of facts. A corollary of this same proposition is that there are circumstances under which it can be said that a subgenus is described by a genus encompassing it and a species upon which it reads. Without necessarily meaning to agree or disagree that agent is the genus, cross-linking antibody is the subgenus, and the exemplified antibodies are "a species" upon which the subgenus "antibody" reads under this rubric, Applicant respectfully asserts that the exemplified antibodies in the specification in fact provide adequate written description support for the cross-linking antibody as claimed.

In the first paragraph on page 7 of the Office Action, the Examiner, citing Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1997), asserted that "entitlement to a filing date does not extend to subject matter, which is not disclosed, but would be obvious over what is expressly disclosed." A clear inference from the Examiner's assertion is that the Examiner does not consider the claimed subject matter to be disclosed, expressly or otherwise. As maintained by Applicant, however, the claimed subject matter in question, namely, cross-linking antibody, is in fact expressly disclosed in Examples 3 and 10. There is no requirement that the claimed subject matter be disclosed *in haec verba* in order to satisfy the written description requirement of 35 U.S.C. 112, first paragraph. In re Gosteli, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Accordingly, such inference cannot be made.

Furthermore, in the third paragraph on page 7 of the Office Action, the Examiner expressly asserted that "The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112." [Emphasis added.] Applicant respectfully disagrees. As pointed out above, there is no requirement that the claimed subject matter be disclosed *in haec verba* in order to satisfy the written description requirement of the first paragraph of 35 U.S.C. 112.

Ibid. The Examples in the specification as filed clearly disclose cross-linking antibodies as currently claimed. Accordingly, such assertion by the Examiner cannot be sustained.

In view of the foregoing, Applicant respectfully asserts that the inventions of claims 4 and 20 find adequate written description support in the specification as filed and therefore requests that the Examiner withdraw the rejection of claims 4 and 20 under 35 U.S.C. § 112, first paragraph, for alleged lack of written description.

Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Beginning with Item 6 on page 7 of the Office Action, the Examiner rejected claims 1, 3, 4, 6-9, 11-13, 17, 19, 20, 22-25, and 38 under 35 U.S.C. 112, first paragraph, for alleged lack of enablement. In the first paragraph on page 8 of the Office Action, the Examiner stated, in part, "[I]n addition to the enablement issues concerning the claimed methods to induce apoptosis in T cells and NK cells with PSGL-1-specific antigen-binding fragments in the absence of administering secondary cross-linking agents / antibodies …". [Original emphasis omitted; shown emphasis added.] Applicant respectfully submits this statement is irrelevant because the claims were previously amended to omit reference to PSGL-1-specific antigen-binding fragments.

Similarly, in the fourth paragraph on page 8 of the Office Action, the Examiner again made reference to "the claimed methods to induce apoptosis in T cells and NK cells with PSGL-1-specific antigen-binding fragments …". [Original emphasis omitted; shown emphasis added.] Applicant respectfully submits this reference is irrelevant because the claims were previously amended to omit reference to PSGL-1-specific antigen-binding fragments.

In addition, Applicant would again like to point out that either secondary cross-linking antibodies or cells expressing Fc receptors (FcR) are capable of cross-linking antibodies bound to PSGL-1 on the surface of T cells or NK cells. As is clear from the specification as filed, administration of cross-linking agents / antibodies is not necessarily required, because, for example, in vivo circulating immune cells bearing FcR can cross-link antibodies bound to PSGL-1 on the surface of cells, in the absence of administering cross-linking agents / antibodies.

Accordingly, narrower claims (such as claim 4) include the limitation of administering cross-linking antibodies, whereas broader claims (such as claim 1) do not recite this limitation.

In the second paragraph on page 8 of the Office Action, the Examiner introduced the notion of "administering multivalent anti-PSGL-1 antibodies, such as diabodies." Applicant would point out that the Examiner has not indicated where such notion is claimed or disclosed in the specification. In fact, in the fourth paragraph on page 9 of the Office Action, the Examiner stated, "[T]he specification as-filed does not appear to provide for multivalent anti-PSGL-1 antibodies as an alternative to adding secondary cross-linking agents / antibodies ...". [Original emphasis.] It is well established patent law that the written description and enablement requirements under the first paragraph of 35 U.S.C. 112 are distinct (see, e.g., Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1560 (Fed. Cir. 1991)) and that an invention can be enabled even in the absence of written description. The Examiner has not provided any basis for his assertion that "administering multivalent anti-PSGL-1 antibodies, such as diabodies" lacks enablement (as opposed to written description).

In the second and third paragraphs under Item 6 on page 8 of the Office Action, the Examiner, citing footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992), asserted that (1) in vitro and animal model studies have not correlated well with in vivo clinical trial results in patients, and (2) pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for certain reasons. As to the former assertion, the Examiner made reference to "therapeutic indices" and "the relative ability or efficacy of the claimed methods ...". Applicant respectfully points out that such considerations are more properly the concern of regulatory approval rather than of patentability, that the claims do not require that the individual is a human, and that it is plainly incorrect to require, generally, human clinical trial results to enable a claim directed to a therapeutic method of treatment.

As to the second assertion above, the Examiner's reliance on Ex parte Aggarwal is clearly misplaced. The claims at issue in Ex parte Aggarwal were directed to a method of treating tumors in animals by the administration of recombinant lymphotoxin. In that decision the examiner's list of reasons why there was a strong likelihood that recombinant lymphotoxin

may not be effective was based on the examiner's citation of prior art references that specifically supported each of the examiner's reasons. For example, two references cited by the examiner in that case indicated that, at the time the application was filed, lymphotoxin had no practical utility against tumors. That is, the examiner in Ex parte Aggarwal provided specific evidence in support of his reasoning in respect of the specifically claimed subject matter. This is in stark contrast to the reasoning provided by the Examiner in the instant application, which, in attempting to assert the same list of reasons as in Ex parte Aggarwal, amounts to mere generalities and speculation. The Examiner has made no attempt to cite any art as specific evidence in support of any one of the reasons drawn from Ex parte Aggarwal. In addition, the appellants in Ex parte Aggarwal submitted a declaration that included an admission that "cancer chemotherapy is an empirical art." In contrast, Applicant in the instant application has made no admission similarly conceding the Examiner's position. Accordingly, Examiner's reliance on Ex parte Aggarwal is misplaced.

In view of the foregoing, Applicant respectfully asserts that claims 1, 3, 4, 6-9, 11-13, 17, 19, 20, 22-25, and 38 are enabled and therefore requests that the Examiner withdraw the rejection of claims 1, 3, 4, 6-9, 11-13, 17, 19, 20, 22-25, and 38 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement.

Provisional Obviousness-Type Double Patenting Rejection

In Item 11 on page 12 of the Office Action, the Examiner provisionally rejected claims 1, 3, 4, 6, 11-13, 17, 19, 20, 22-25, and 38 under the judicially created doctrine of obviousness-type double patenting over claims 1, 4, 8, 9, 12-15, 19-22, 23, 26, 30, 31, and 34-38 of copending application USSN 10/662,906. In response, Applicant calls the Examiner's attention to the fact that claims 1, 4, 8, 9, 12-15, 19-22, 23, 26, 30, 31, and 34-38 of copending application USSN 10/662,906 have been canceled. Accordingly, Applicant respectfully requests that the Examiner withdraw the provisional obviousness-type double patenting rejection of claims 1, 3, 4, 6, 11-13, 17, 19, 20, 22-25, and 38 patenting over claims 1, 4, 8, 9, 12-15, 19-22, 23, 26, 30, 31, and 34-38 of copending application USSN 10/662,906.

Withdrawn Claims

As noted above, claims 7-9 are currently withdrawn from consideration as being directed to nonelected species. Applicant respectfully reminds the Examiner that Applicant is entitled to consideration of these claims if all claims directed to the elected invention are in condition for allowance. MPEP 821.04; Office Action dated February 25, 2004. Each of withdrawn claims 7-9 is dependent from claim 1, which the Examiner previously indicated is generic.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No. A0871.70000US01.

Dated: May 29, 2008

Respectfully submitted,

By_____

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